PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (see an example) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below. Some articles will have been accepted based in part or entirely on reviews undertaken for other BMJ Group journals. These will be reproduced where possible.

ARTICLE DETAILS

TITLE (PROVISIONAL)	A Brief Intervention for Drug Use, Sexual Risk Behaviours, and Violence Prevention with Vulnerable Women in South Africa: A Randomised Trial of the Women's Health CoOp
AUTHORS	Wechsberg, Wendee; Jewkes, Rachel; Novak, Scott; Kline, Tracy; Myers, Bronwyn; Browne, Felicia; Carney, Tara; Morgan Lopez, Antonio; Parry, Charles

VERSION 1 - REVIEW

REVIEWER	Dr Vctoria Allgar Senior Lecturer University of York
REVIEW RETURNED	30-Jan-2013

THE STUDY	There was a range of outcome measures. The primary outcome was later described as biologically confirmed abstinence from drug use at 12 months. There was a power calcultion. However it would be clearer if the study was powered on this outcome, rather than a range of effect sizes for multiple outcome measures. It was not clear why randomiastion was undertaken on a 2:1:1 basis. The flow-chart of randomisation numbers and missing data is useful. It was not clear why there were more patients at 12 months than at 6 months. The statistical analysis approach seems over complicated, and in the results it was difficult to assertain what tests were used to make the comparisons.
RESULTS & CONCLUSIONS	In Table 2 the groups are anlaysed individually (F-Test for Trend (2df)). There needs to be a comparsion betwen groups rather than within groups. In figure 2, the majority of the odds ratios cross 1, with the exception of the primary outcome. "At the 12-month endpoint, 26.9% of the participants in the WHC arm were abstinent compared with 16.9% in the Nutrition arm and 20.0 % in the HCT-only control arm." A simple chi-square test could be used here to compare the three groups, followed by a logistic regression model to compare groups and control for baseline data and confounders (race, centre)? No adjustments were made for multiple significance testing.

REVIEWER	Robert Morrell (PhD) Coordinator, Programme for the Enhancement of Research Capacity (PERC), Research Office, University of Cape Town, P/Bag,

	Rondebosch 7701, South Africa. I have worked with Professor Rachel Jewkes, the second author. I do not know the other authors. I do not have a conflict of interest.
REVIEW RETURNED	18-Feb-2013

GENERAL COMMENTS	Coming as I do from a Social Science background, I don't find the rather prescriptive format of these forms very easy so I am taking the liberty of putting in my comments below (in longhand, to use an old term!). Description Useful and unusual (in the African context) evaluation exercise that focuses on drug-taking women and tries to see if a short term ('brief') health intervention reduces drug taking and HIV risk, as well as risk of violence associated with sex. Intervention developed in the US and applied successfully with sex workers in Pretoria. It is now being tested in a different group of women in a different (and dangerous) setting (western cape). Thorough and important – it is very important that this kind of research is undertaken and fed back into policy to make a real impact on a range of serious social problems and to support the intended at-risk group (drug-taking adult women of low economic status). Modest and realistic findings made about the efficacy of the brief intervention. Refreshing and useful. 16/33 "This study is possibly the first RCT of a brief intervention to reduce women's drug use after 12 months in an HCT field setting in Africa." Yes, and therefore worthy of publication. Small points: 6/33 "A strength is only 8.1 of the sample was lost to follow up." (Presumably 8.1%) Correction There needs to be some explanation (a sentence would do) of why the 3 and 9 month test results were not used. ie some justification for using 6 and 12 month tests. 15/33 "There was a pattern of significant changes over the 3 time points, with an increase in the number of participants" Which three time points – earlier the authors said that they were only considering TWO time points. Observations Methods - Methodical and fine. The modules are very rationalist, assuming that much of what goes on in relationships is an effect of voluntarist and individual practice. While this is problematic (ie does NOT explain how relationships are in fact conducted), it is also obviously the case that education can influence decision making even when it does not impact on gender equality or relational dynamics. It should not be a surprise when interventions that rely on

	linear assumptions about behaviour change are not long-lasting. 17/33 “The reduction in biologically measured drug use was mirrored in trends of declining drug-impaired sex at 6 months, which is potentially important for HIV prevention. However, this trend was not sustained at 12 months post intervention.” Yes, see my earlier reservation about the transmission/knowledge orientation of the intervention. 18/33 “In high-income countries, brief screening interventions for alcohol abuse have been shown to be effective in primary healthcare settings,11 but such interventions for other drug use have been researched very little.[25] To our knowledge, this is the first time a brief intervention has been shown in an RCT to be of use in an HCT setting in a low-to-middle–income country and among female drug users a year later. Further, this intervention was implemented among a group of vulnerable women and can be easily translated into other hard-to-reach settings” The caveat here would be, as with many of such education approaches, that behavioural change is difficult to effect purely by the kinds of input offered in this brief intervention. On the other hand, the results suggest that some of the participants were ‘reached’ in the process and ‘empowered’. It would help to have a slightly better sense of who these people were and why they changed and maybe this should be the object of future research. Point for reflection. The salience of gender inequality is asserted though it is not easy to see from this study what its effect actually is. This is relevant in a policy field which increasingly tackles public health issues with an integrated approach to gender that includes consideration of men and masculinity. This doesn’t mean that interventions that work exclusively with women are inappropriate but I think it does mean that authors should acknowledge the possible limitations of such a selection of target audience. Questions I’d be interested to see if there are any significant findings across ‘race’. In the Western Cape (and much of South Africa) ‘race’ is often proxy for different histories, community experiences and living circumstances. And were the participants asked if they had a criminal record? If not, any explanation why not? The three imprisonments noted suggests quite high levels of involvement in crime. I would have thought the intervention might be more effective among better educated participants who were not involved in crime (and it would be interesting to see if this hypothesis is correct).

REVIEWER	Abigail M Hatcher Senior Researcher University of California, San Francisco USA I have no competing interests.
REVIEW RETURNED	04-Mar-2013

GENERAL COMMENTS	This trial is an important addition to the evidence-based intervention (EBI) literature, in that it tests a U.S.-developed model for preventing HIV, violence and substance abuse in a South African population of drug-using women. However, there are several shortcomings that should be addressed by the authorship team to prepare this manuscript for publication. The key strengths of the research – that the intervention has been tested elsewhere, carefully adapted for use in South Africa, and examines pre-defined study endpoints – have been weakened somewhat in an attempt to present the study findings in a positive light. I would encourage the authors to report the mixed research findings in a more robust manner, using the ineffectuality of the HIV prevention aspects of the intervention as a building block for future studies. Cathy Campbell's work comes to mind as an exemplary set of publications that used intervention pitfalls productively by highlighting potential challenges. I believe these rather significant changes to the manuscript can be achieved by filling the BMJ Open word space (up to 4000 words, currently the paper is 3364) with a better description of Results and a more thorough Discussion. Introduction 1. You briefly discuss the guiding theories of the intervention as being feminist and empowerment-oriented. Are information-motivation-behavioral theories not also central to this type of intervention? Study Design 2. Please list sexual behavior and victimization as primary outcomes, as per the study protocol. 3. Briefly, how did you adapt the U.S. intervention to the needs of South African participants, based on your formative research? Results 4. In the body of the text, kindly present the effect of the intervention on protection with main partner, protection with casual partner, casual partners, experience of physical IPV. Limitations 5. Briefly, why was enrolment in the trial slow (such that you did not reach anticipated n=900 participants)? Please state that this limited your power to detect effect sizes on primary outcomes of interest. 6. It would be useful to expound upon your choice of a biological indicator for substance use but not incident HIV infection. Discussion It is important for the field that you critically examine the insignificant study findings in addition to suggesting further applications for its significant findings. I encourage the authors to consider the following discussion points, in light of existing literature: 1. Kindly compare these findings to previous iterations of this intervention in the U.S. and Pretoria. I believe other publications of this authorship team have had more success, and am curious

	whether there was something particular about the study setting/population that precluded similar results? 2. Why might there have been so little intervention effect on primary study outcomes of sexual behavior and victimization? Did your experience lead you to believe this was a failure of the intervention itself or a shortcoming in the delivery methods? 3. Please reflect on the study's HIV and violence findings in light of other South African interventions that show measurable reductions in sexually risky behavior (many studies exist, including your own) and victimization (you mention one study that was successful, Pronyk et al. (2008)). How did these approaches differ from yours, and what might the HIV and violence fields learn from these differences? 4. In a setting where violence and alcohol abuse are endemic, how did you choose to focus on individual behavior change rather than broader social/structural factors that predict substance abuse and victimization? This is an interesting theoretical choice given the evidence that sexual behavior does not operate within the information-motivation-behavioral model when violence in the relationship exists (eg. Mittal (2011) Aids & Behavior). How did you balance the individualist approach of this intervention (eg. asking women to "protect themselves from violence, to negotiate condom use with sex partners, and to take control over their drug use.") with the communal and social characteristics of South African society? 5. I'm curious what the authors mean by "hard-to-reach settings" (P 18, line 27)? Geographically, the study was conducted in Cape Town, which has few similarities to other settings in South Africa, and fewer still to other settings in sub-Saharan Africa. Population wise, the study was conducted among drug using women, which is indeed a hard-to-reach population. It would be interesting to note how this sample choice framed the study recruitment methods and substandard enrolment rate. 6. On P 17, line 20 the authors state: "Nonetheless, the gender sessions of the WHC intervention may have been of considerable value to women." Did the authors collect acceptability data that supports this statement, and will be subsequently reported elsewhere? If not, I would encourage them to remove this statement or support it by other literature. 7. Following the statement on P 18 line 32: "this brief intervention has the potential for broader dissemination," please add the phrase "among drug using populations elsewhere."

VERSION 1 – AUTHOR RESPONSE

Reviewer 1: Dr Victoria Allgar
Response:Thank you so much for your suggestions, especially around the statistical analyses in the paper.
Reviewer 1: Primary outcome was described as biologically confirmed abstinence. The study should be powered on this outcome, rather than a range of effect sizes for multiple outcome measures
Response: The study was powered on this primary outcome and the range for other outcomes for the secondary outcomes have been removed.
Reviewer 1: Unclear why randomization was undertaken on a 2:1:1 basis

Response: The study was powered so that half the sample could benefit from the women's intervention. We have added a line in the manuscript.
Reviewer 1:Unclear why there were more patients at 12 months than at 6 months
Response: After some of the clients missed their 6 month follow up appointments and were presumed to be lost to follow up, we managed to track them and locate them for their 12-month follow up appointment. An additional comment has been added to the text of the journal article to explain this (page 15).
Reviewer 1: The statistical analysis seems over complicated, and difficult to ascertain what tests were used to make the comparisons
Response: We recognize that the analyses contain a lot of technical details that may not be clearly understood by non-technical reviewers. We have tried to link specific analytic tests to specific tables and research questions to help inform the less statistically sophisticated reviewer. However, we felt that it was imperative to keep the level of detail so that anyone seeking to replicate our findings, either with our data or their own data, could sufficiently re-create specific variables and analyses.
Reviewer 1: Table 2: the groups were analysed individually, but there needs to be a comparison between groups.
Response: The groups were indeed analysed together in a single model, with coefficients representing the statistical difference in the effect for condition, time, and time by condition. For the condition effect, the conditions were tested (a) each condition against the other conditions; and (b) each condition against the combined effect. The results did not change appreciably between both strategies.
Reviewer 1: Figure 2: a chi-square test can be used to compare the WHC, nutrition and HCT-only groups, and then a logistic regression model to compare groups and control for baseline data and confounders.
Response: Our analyses were estimated within a generalized linear mixed model, which allows us to retain missing data at either follow-up wave. Using a standard logistic model would remove those cases under the listwise deletion assumption, and therefore, we would not be making full use of all deployable data.
Reviewer 1: No adjustments were made for multiple significance testing.
Response: Typically, corrections are employed for observational data when there are little/no a priori hypotheses. This study was powered to detect a specific set of outcomes by intervention condition and no specific post-hoc corrections were necessary. It is very rare for a randomized clinical trial to use multiple testing corrections for a primary outcome analyses. We have confirmed guidance on this issue here: Shaffer, J. P. "Multiple Hypothesis Testing." Ann. Rev. Psych. 46, 561-584, 1995.

Reviewer 2: Robert Morrell
Response: Thank you so much for the support of our work and your valuable comments.
Reviewer 2: A strength is only 8.1 of the sample was lost to follow up. Presumably 8.1%
Response: The reviewer is correct and we have made this correction to the text of the article (page 6)
Reviewer 2: There needs to be some explanation of why 3 and 9 month test results were not used
Response: A sentence has been added to address this issue (see page 12)
Reviewer 2: There was a pattern of significant changes over the 3 time points, earlier the authors said that they were only considering two time points
Response: We only considered two time points, this error has been corrected in the text of the article (page 16)
Reviewer 2: Methods: Interventions that rely on linear assumptions about behaviour change are not generally long-lasting
Response: We acknowledge that brief interventions generally lack sustainability and cannot address structural contributors to complex psychosocial problems. We highlight this in the discussion as well as the need for future studies to examine structural and contextual determinants of behaviour change.
Reviewer 2: Trend for reduced impaired sex was not sustained at 12 months follow up
Response: We agree with this feedback, and note issues around sustainability in the discussion

Reviewer 2: It would be helpful to have a better sense of who these people were and why they changed. Maybe this should be the object of future research.
Response: While we did not address this in the current study, future research will address who the particular interventions have been successful for.
Reviewer 2: The issue of gender inequality is asserted but it is difficult to consider men and masculinity when the target audience is women.
Response: This has been added to the limitations section: future work should be with couples, not just women
Reviewer 2: Were there significant findings across race
Response: The study was not powered for specific differences by racial categories (Blacks versus Coloured). We did add a control variable in the model in an exploratory phase and found that the study effects remained in the same direction and level of significance. Therefore, the intervention appears to affect both races. In the presentation of our findings, we chose not to include these findings to simplify the reporting of our results, and because the racial differences were not part of a pre-specified test.
Reviewer 2: Were participants asked if they had a criminal record
Response: We ask about activities and incarceration and we have published a paper (reference 22) addressing these issues.

Reviewer 3: Abigail Hatcher
Response: Thank you for your thorough and thoughtful review of the article. We have written much more and are slightly over the 4000 words.
Reviewer 3: Mixed research findings to be presented in a more robust manner-look at Cathy Campbell's work
Response: We agree that this kind of work like Cathy Campbell's is bottom-up with mixed methods. We also note sometimes results do not turn out as expected. We mention the earlier studies and more about mixed results in the discussion, as well as to the original intervention with sex workers with having higher risk behaviours. In community research, we have found it is difficult to truly isolate confounding on every study outcome. Therefore, additional studies are needed to replicate these findings and enhance generalizability. We are continuing to analyse these data for several additional manuscripts.
Reviewer 3: Briefly discuss guiding theories of intervention as being feminist and empowerment-orientated. Are information-motivation-behavioral theories important?
Response: Social-cognitive theories are a very important part of the empowerment framework and feminist theory. We teach knowledge and assertive skills in the intervention. We clarified the framework in the manuscript.
Reviewer 3: List sexual behavior and sexual victimization as primary outcomes, as per the study protocol
Response: The study was powered to focus on several key study outcomes and several outcomes papers. In subsequent papers, we plan on devoting separate scientific analyses to those outcomes and their mediating/moderating pathways.
Reviewer 3: How was US intervention adapted to the needs of the South African participants, based on your formative research
Response: Focus groups and a pilot study were conducted before this RCT started. This has been added to the section on the intervention and the references published about these adaptations.
Reviewer 3: Present the effect of the intervention on protection with main partner, casual partners, experience of IPV
Response: These are very important outcomes and the papers addressing these outcomes are forthcoming.
Reviewer 3: Why was enrolment in the trial slow, and comment that this limited your power to detect

effect sizes on primary outcomes of interest
Response: In the methods section of the paper (pages 8-9), we further explain the detailed and methodologically rigorous sampling plan used. We also describe why enrolment was slow
Reviewer 3: Useful to expand upon choice of a biological indicator for substance use but not incident HIV infection
Response: This is a very interesting point. However, it is not the focus of the current paper. Incident HIV will be examined in a subsequent paper but we never powered this study on HIV as an outcome variable.
Reviewer 3: Compare findings to previous literature on this intervention in US and Pretoria
Response: This study is set in a very different context. Cape Town is different than Pretoria, particularly in terms of drug use. We have added a sentence or two to the introduction and discussion highlighting the contextual differences between these settings.
Reviewer 3: Comment on lack of intervention effect on primary study outcomes of sexual behaviour and victimization
Response: We think that environmental issues played a role in the success of the intervention, and also long-standing gender norms that are difficult to change. We have added a section to the discussion highlighting this.
Reviewer 3: Reflect on study's HIV and violence findings compared to other South African interventions e.g. Pronyk et al, 2008
Response: The Pronyk et al study utilised a different population and also did not take into account drug use, which is known to be related to sexual risk.
Reviewer 3: How was the decision made to focus on individual behavior
Response: The intervention was delivered in a group format to build 'sisterly support' but women still live in single household, although many shacks, in these communities. We have noted the limitations to the individual focus in the discussion
Reviewer 3: What is meant by hard to reach settings, and how did the sample choice of drug-using women frame the study recruitment methods and enrolment rate
Response: We agree with the reviewer and have clarified hard-to-reach populations of drug-using women in the article (see page 20)
Reviewer 3: On page 17, line 20: did authors collect acceptability data on the value of gender sessions of the WHC intervention to women
Response: This data was collected by conducting in-depth interviews with women from the WHC intervention, as well as by the anonymous comments made by women in the study's comment book. This paper is currently going under review.
Reviewer 3: On page 18, line 32: Please add phrase "among drug-using populations elsewhere" after "this brief intervention has the potential for broader dissemination".
Response: This has been added in the text.

VERSION 2 – REVIEW

REVIEWER	Hatcher, Abigail Universiy of California, San Francisco, Bixby Center for Global Reproductive Health
REVIEW RETURNED	17-Apr-2013

GENERAL COMMENTS	Thanks to the authors for their response. I believe the manuscript has been strengthened in this revision, and am supportive of its publication.